Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claim 1 has been amended, claims 3-4 have been cancelled without prejudice, and new claims 10-21 have been added. Descriptive support for new claims 10 and 11 appears in the first full paragraph on page 30 and the third full paragraph on page 35, respectively; descriptive support for new claims 12-14 appears in the first full paragraph on page 34; and descriptive support for new claims 15 and 16 appears in the first full paragraph on page 30. New claim 17 finds descriptive support in original claim 3 (i.e., claim written in independent form), and new claims 18-21 find descriptive support in original claims 6-9, respectively. Claims 1, 2, and 5-21 are pending.

The objection to the specification is overcome by the above amendments. Although applicants disagree with the assertion made by the U.S. Patent and Trademark ("PTO"), the present claim language is clearly supported by the first full paragraph on page 30, along with the disclosure of the nucleic acid sequence of SEQ ID NO: 183 and the corresponding amino acid sequence of SEQ ID NO: 184.

The objections to claims 1, 3, and 4 are overcome by the above amendments and should be withdrawn.

The rejection of claim 5 under 35 U.S.C. §112 (second paragraph) for indefiniteness is respectfully traversed. The PTO has taken the position that the term "purified" is unclear in view of the language "isolated" as used in claim 1. Applicants respectfully disagree.

The term "isolated" connotes that the claimed subunit is in an environment that is distinct from that of the native subunit, i.e., the subunit no longer exists in a cellular environment. In contrast to a polymerase subunit that can exist, for example, in a protein extract obtained from a cell, a purified polymerase subunit is one that is substantially separated from other proteins. By way of example, both isolated polymerase subunit and purified polymerase subunit are described in the procedure recited in Example 18 for the recombinant expression of *A. aeolicus* alpha (*dnaE*) subunit. In particular, Example 18 describes cell lysate containing the recombinant polymerase subunit (i.e., isolated but not yet purified protein), as well as the purification of polymerase subunit from the cell lysate (first

via Sepharose column and then via Heparin Agarose column). Thus, "purified" and "isolated" are distinct terms, and persons of skill in the art would understand the distinction between these two terms.

For these reasons, the rejection of claim 5 is improper and should be withdrawn.

The rejection of claims 1, 2, and 4-9 under 35 U.S.C. §112 (first paragraph) as lacking written descriptive support is respectfully traversed.

The burden of establishing that an application lacks adequate written descriptive support falls on the PTO. *See In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims."). Hence, the PTO must demonstrate *why* the disclosure is insufficient.

The Federal Circuit has clearly espoused that *per se* conclusions of written description violations cannot be founded upon the basis of genus size alone. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1326-27, 63 USPQ2d 1609, 1614-15 (Fed. Cir. 2002) (refusing to adopt position that three species as a matter of law cannot satisfy written description requirement for significantly larger genus). Thus, the PTO's conclusion cannot be based on genus size alone. But that is precisely what the PTO has done at page 4 of the outstanding office action. Because the PTO's position is unsupported by law and unsupported by any facts other than genus size, applicants submit that the PTO's position cannot be sustained.

In contrast, applicants present Exhibits 1-3 (attached hereto) as evidence that the nucleic acid sequence of SEQ ID NO: 183 and the corresponding amino acid sequence of SEQ ID NO: 184 represent the claimed genus. Exhibit 1 is a presentation of a Genbank accession for a thermophilic *Bacillus*, or *Geobacillus*, *polC* nucleic acid that is homologous to the nucleotide sequence of SEQ ID NO: 183. This *polC* nucleic acid was identified by a protein-protein BLAST search of the Genbank database performed using the amino acid sequence of SEQ ID NO: 184 and the BLAST default settings. Homologous sequences were identified in a number of *Bacillus* species, including from the thermophile *Geobacillus kaustophilus* (Exhibit 1). Based upon alignments performed using Align® for nucleic acids and ClustalW for amino acids (using the European Molecular Biology Laboratory server and its default settings), this homolog shares about 99 percent identity at the nucleic acid level (Exhibit 2) and about 99 percent identity at the amino acid level (Exhibit 3). Thus, species of

PolC subunits from thermophilic organisms that belong to the biological classification *Bacillus*, or *Geobacillus*, clearly share similar structure and, therefore, function.

Applicants submit that the language recited in claims 1 and 2 is precisely the type of claim language that was acknowledged in *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) as being acceptable under the written description requirement. In *Eli Lilly*, the Federal Circuit addressed the validity of several claims of U.S. Patent No. 4,652,525 to Rutter et al. ("Rutter"), specifically those claims that recited the limitations 'vertebrate,' 'mammalian,' or 'human' cDNA for insulin. Rutter disclosed the nucleotide and amino acid sequences of a rat cDNA encoding insulin, and described a general procedure for obtaining the human cDNA encoding insulin. *Id.* at 1567, 43 USPQ2d at 1405. The Federal Circuit found that the description of the rat cDNA did not provide adequate descriptive support for the narrow subgenus of 'human' cDNA (no species disclosed), the larger subgenus of 'mammalian' cDNA (only the one rat species disclosed), and the larger genus of 'vertebrate' cDNA (only the one rat species disclosed). *Id.* at 1567-68, 43 USPQ2d at 1405. The Federal Circuit did acknowledge, however, the district court's statement that the specification provided adequate written descriptive support for the subgenus of 'rat' cDNA encoding insulin. *Id.* at 1566.

Thus, functional language should be acceptable when the genus as claimed is sufficiently limited in scope (i.e., from *Bacillus* or *Bacillus stearothermophilus*) and the specification describes one or more species within that genus. Claims 1 and 2 recite the same type of functional claim language that was identified as acceptable in *Eli Lilly* given the description of a single species by its nucleotide sequence. Thus, it should be evident that claims 1 and 2 (and claims dependent thereon) find written descriptive support in the present application.

The conclusion by the PTO is contrary to evidence submitted herewith by applicants. One of ordinary skill in the art would have understood that applicants were in possession of the presently claimed invention at the time the present application was filed. This is so, because persons of skill in the art would have expected sufficiently related thermophilic organisms from the genus *Bacillus* (and now *Geobacillus*) to possess homologous *polC* nucleotide sequences or thermostable PolC subunit proteins. Exhibits 1-3 confirm this expectation to have been reasonable.

In view of all of the foregoing, applicants submit that the rejection of claims 1, 2, and 4-9 is improper and should be withdrawn.

The rejection of claims 1, 2, and 4-9 under 35 U.S.C. §112 (first paragraph) for lack of enablement is respectfully traversed.

It is the position of the PTO that the specification does not provide sufficient guidance for making and using other PolC subunits within the scope of the claims. Applicants respectfully disagree.

The PTO is respectfully reminded that all that is needed is objective enablement of what is claimed. *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The present application provides the nucleotide sequence of *Bacillus* (now *Geobacillus*) *stearothermophilus polC* (e.g., SEQ ID NO: 183) and its corresponding amino acid seqeuence (e.g., SEQ ID NO: 184), and describes how one of ordinary skill can isolate homologs of the disclosed sequence (*see* page 41, line 9 to page 42, line 29), express the PolC subunit encoded by such homologous *polC* sequences (*see* Example 18, expressing *A. aeolicus* alpha subunit), and test the encoded polymerase subunit for Pol III assembly competence (*see* Example 25, testing *A. aeolicus* polymerase assembly with clamp loader) and for polymerase activity (*see* Examples 26 and 30, testing *A. aeolicus* polymerase activity). Thus, one of ordinary skill in the art would have been fully able to make and use DNA molecules and their encoded proteins within the scope of the presently claimed invention.

Moreover, with regard to method 3 for homolog identification, described at page 42, that is precisely the approach used to identify the *polC* homolog shown in Exhibit 1. For this reason, it should be apparent that the present application fully enables the production and use of other species of *Bacillus or Bacillus (*now *Geobacillus*) *stearothermophilus* PolC homologs.

In view of all of the foregoing, applicants submit that the rejection of claims 1, 2, and 4-9 for lack of enablement is improper and should be withdrawn.

Because 1 is allowable for the reasons noted above, applicants further submit that new claims 10-16 also are allowable. Consistent with the PTO acknowledgments at pages 3-4 the outstanding office action, and consistent with the identification of claim 3 as allowable, applicants further submit that claims 17-21 are allowable because claim 3 is now presented in independent form as claim 17.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: September 28, 2006

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